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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KOLKER, DANIEL E

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,342	DESNOYERS ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 Dec 2001, 4 Sep 2002, 14 Oct 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22-34* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/24/04, 5/3/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendments filed 26 December 2001 and 4 September 2002 have been entered. Claims 22 – 34 are under examination.

Priority

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

The preliminary amendment filed 4 September 2002 indicates that this application is a continuation of 09/931836, which is a continuation of PCT/US00/05601, which claims priority to provisional application 60/130359, filed 21 April 1999. While applicant disclosed the amino acid sequence in said provisional application, no use for the protein was disclosed.

Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the provisional application filed 21 April 1999 does not meet the requirements of 35 U.S.C. § 112, first paragraph, it is unavailable under 35 U.S.C. § 119(e). The effective priority date of the instant application is considered to be the filing date of the international application PCT/US00/05601, filed 1 March 2000.

The examiner has determined that the asserted utilities, i.e. the positive results in assays 106 (Detection of Polypeptides that Affect Glucose or FFA Uptake in Skeletal Muscle) and 92 (Mouse Kidney Mesangial Cell Proliferation Assay), do not constitute specific and substantial utilities as required under 35 U.S.C. § 101. The reasons for this determination are enumerated below.

Should applicant argue that the provisional application filed 21 April 1999 in fact is an enabling disclosure, applicant must specifically indicate the page and line numbers where PRO4380 was found to test positive in assays 92 and 106, as well as overcome the rejection under 35 U.S.C. § 101 below.

Information Disclosure Statement

The information disclosure statements filed 3 May 2002 and 24 June 2004 have been considered. The database search results demonstrate that applicants are aware of nucleic acids with identity or homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the examiner cannot determine if said sequences constitute prior art.

Specification

The disclosure is objected to because of the following informalities:

The title is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The specification includes browser-executable hyperlinks. This objection could be overcome by deleting all occurrences of the text "http://".

Appropriate correction is required.

Claim Rejections - 35 USC §§ 101 and 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22 – 34 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The polypeptide of the instant application has been isolated because of its similarity to a known protein. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct,

1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The claims are drawn to isolated polypeptides, called PRO4380, as well as variants at least 80% identical thereto fragments of same, and chimeric polypeptides. The specification asserts that PRO4380 has two specific utilities, as it came up positive in two assays, however neither utility is substantial.

The research data presented in the instant specification indicate that PRO4380 of SEQ ID NO:57 "tested positive as either stimulator[s] or inhibitor[s] of glucose and/or FFA uptake" in an assay using primary rat differentiated skeletal muscle (page 166, Example 37). Based on the results of the assay disclosed in the Example 37 it was asserted that the instant PRO4380 polypeptides "would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia" (page 166, lines 17 - 19). However, based on the information supplied in the instant disclosure, one skilled in the art would clearly not know what is the specific utility of the instant PRO4380 with respect to glucose or FFA uptake. The specification (p. 166) discloses that a protein is scored as a 'positive' in the glucose and FFA uptake assay if any one of four conditions is met:

a) Glucose uptake decreases by at least 50% from control

b) Glucose uptake increases to at least 150% of control

c) FFA uptake decreases by at least 50% from control

d) FFA uptake increases to at least 150% of control

But the specification does not indicate which of the above-listed conditions applies to PRO4380. Is it stimulation or inhibition of glucose uptake? Would PRO4380 polypeptides be useful to treat hyper-insulinemia or hypo-insulinemia, two opposite conditions? Or would it be useful in stimulating or inhibiting glucose uptake?

Furthermore, the observed differences do not appear to be statistically significant and the cutoff points appear to be arbitrary and there is not obvious scientific basis for them. For example, Santomauro et al. (1999. Diabetes 48:1836-1841) teach that 56.5% decreases in FFA levels are statistically significant and correlated with physiological improvements, but it is not clear from either the prior art or the specification whether 50% decreases are useful (see Table 2 from Santomauro et al.). Note that 50% decreases in *plasma* insulin do appear to be significant, but it is not clear whether this is due to a doubling of insulin uptake by skeletal muscle or by other tissues, or whether it is due to changes in the amount of insulin production. Similarly, the observation that 56.5% decreases in *circulating* FFAs is significant and correlated with physiological improvements does not indicate that a doubling of uptake of FFAs *by skeletal muscle cells* will lead to the same decreases in FFAs. For example, doubling the amount of FFA uptake from 1% to 2% of total circulating FFAs would not be expected to lead to a 56% decrease in circulating FFA levels. It is unclear to the examiner why one would want to decrease FFA uptake, as that would be expected to result in higher circulating FFAs, which can lead to diabetes (see Santomauro et al., p. 1836, second column, last sentence of first paragraph). Additionally Boden (2003. Exp Clin Endocrinol Diabetes 111:121-124) teaches that increasing plasma FFA leads to atherosclerosis (p. 123, first column, under Summary). Additionally, it is not clear from either the prior art or the post-filing art that FFA uptake is a useful assay. Boden teaches that there is not a cause and effect relationship between FFA-mediated changes in intramyocellular triglyceride content and changes in insulin resistance (p. 122, first column, in the middle of the first full paragraph). Kelley et al. (1999. Am J Physiol 277 (Endocrinol Metab 40):E1130-E1141) teach that free fatty acid uptake may not be as important in determining obesity as other factors, such as fatty acid oxidation (see p. E1139, second column first full paragraph).

35 USC § 101 specifically requires that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. Because the instant specification, as filed, fails to disclose a specific role of PRO4380 in glucose and/or FFA uptake, one would have reasons to conclude that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form.

The data presented in Example 41 (p. 168 – 169) of the specification indicate that PRO4380 was positive in the Mouse Kidney Mesangial Cell Proliferation Assay. It is

acknowledged that proliferation of mammalian kidney mesangial cells is useful. However, the threshold used in determining whether a particular PRO molecule counts as "positive" in this assay would not be considered reasonable by one of skill in the art. The specification discloses (p. 169, lines 1 – 2) that positives in this assay include anything which is at least 15% over the control reading. The post-filing publication by Rovin et al. (2002. Kidney International 61:1293-1302) indicates that a 21% increase in human mesangial cell proliferation is not statistically significant (see particularly p. 1296, lines 3 – 6). Note that the assay used by Rovin et al. is similar to that disclosed in Example 41: both used the Cell-Titer 96 reagent from Promega, measured absorbance at 490 nm, and expressed the results as the ratio of the absorbance for a given treatment to that of control cells (see Specification, p. 168 – 169, and Rovin et al., p. 1294, second column, second complete paragraph). Because the specification does not disclose the degree to which PRO4380 increased cell proliferation, or whether or not the results were statistically significant, the teachings of Rovin et al. indicate that PRO4380 is not useful in the proliferation of kidney mesangial cells. Clearly, further research and experimentation are required to find out whether the PRO4380 is useful as asserted.

A substantial utility, *by definition*, is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility. In the instant case, the mere fact that PRO4380 was "positive" in two assays is at the most, an interesting invitation for further research, experimentation and confirmation as to whether the PRO4380 is useful as a treatment for hyper-insulinemia, hypo-insulinemia, or kidney mesangial cell proliferation. The further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered specific or substantial.

Claims 22 - 34 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if PRO4380 had utility and were enabled, enablement would not be commensurate in scope with claims 1 - 5 because the specification does not reasonably provide enablement for polypeptides 80%, 85%, 90%, 95%, or 99% identical to SEQ ID NO:57. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731 737, 8 USPQ2d 1400 1404 (Fed. Cir. 1988).

The claims are directed to isolated polypeptides having at least 80% identity to a SEQ ID NO:57 with or without its signal peptide, or to polypeptides at least 80% identical to the extracellular domain of SEQ ID NO:57 with or without its signal peptide. Dependent claims are directed to chimeric polypeptides. The specification contains numerous asserted utilities including the identification of molecules that bind to PRO4380 (including agonists and antagonists), as molecular weight markers, therapeutic agents, and for the production of antibodies. None of these asserted utilities is specific for the disclosed PRO4380 protein, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO4380.

Because the claimed nucleic acids are described at least in part in terms of the protein that might be encoded, the scope of the protein itself must be considered: The specification (p. 155, lines 29 – 33) teaches that the nucleic acid encoding PRO4380 has (unspecified) homology to the nucleic acids which encode CER11H6_1, S56299, D89150_1, G70870, S43914, LMO34616_5, LLU78036_1, AF055904_2, P W79066 and ARGE_ECOLI however the instant specification fails to indicate the degree of homology thereto. The specification (Figure 26) discloses that the amino acid sequence might contain a transmembrane domain, but does not indicate which end of the protein is the intracellular domain and which is the extracellular domain.

The Examiner has determined that polypeptides identical to PRO4380 do not meet the utility requirements of 35 U.S.C. § 101, as detailed above. The claims encompass an unreasonable number of inoperative polypeptide sequences, which the skilled artisan would not know how to use. As opposed to the claims, what is disclosed about PRO4380 is narrow: a single polypeptide with no known significance or function and hence no inventive utility.

There are no working examples of polypeptides less than 100% identical SEQ ID NO:57. The examiner has determined that the asserted utilities are not sufficient to meet the requirements of 35 U.S.C. § 112, first paragraph. While the specification generally describes properties of cytokines, it is acknowledged that cytokines are diverse in function and structure. The specification does not provide guidance for using polypeptides related to (i.e., 80%-99% identity) but not identical to SEQ ID NO:57 which do not have the activities that PRO4380 is asserted to have. However, the instant specification discloses, a single isolated polypeptide sequence SEQ ID NO:57.

Furthermore, protein function cannot be reliably predicted from sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does not allow predictability in this instance. Absent a clear disclosure of which elements of PRO4380 are required for its activity, the claims to fusion proteins and variants that are related only by percentage of sequence identity are not fully enabled.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of proteins and lack of knowledge about functions of encompassed polypeptides structurally related to SEQ ID NO:57, the potential one limited working example of nucleic acid encoding PRO4380 and its two asserted functions without correlation between any structural elements and the asserted functions, the lack of direction or guidance for using either polypeptides that are not identical to SEQ ID NO:57, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

The examples provided in the specification do not provide a representative number of different amino acid sequences that would enable a representative number of the above discussed sequences with assurances that they possess the desired activity. The mere

recitation of this term, and the definitions provided do not serve as sufficient guidance to enable the breadth of the claims for the various amino acid sequences claimed. See *Ex parte Forman*, 230 USPQ 546. Since the first paragraph of the statute under 35 U.S.C. § 112 requires that there must be an enabling disclosure to support the breadth of the claims, a review of the specification confirms that the scope of the various amino acid sequences that are discussed above have not been enabled. There is but a single amino acid disclosed with reference to PRO4380, SEQ ID NO:57. In the absence of sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the claims.

Claims 22 - 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R § 1.808(a)). Examiner acknowledges the deposit of organisms under accession number ATCC 203018 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, in order to be fully compliant with the requirement, applicants must state that the deposit will be maintained for a term of at least 30 years and *at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository.* See 37 C.F.R. § 1.806.

Claims 22 – 27, 30, 31, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 22 - 26 are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. Dependent claims 12 and 13 are drawn to chimeric polypeptides comprising sequences at least 80% identical to the disclosed sequence. The claims do not require that the claimed polypeptide possess any particular

biological activity, and while claims 22 – 27, 30, and 31 recite "the extracellular domain" of the protein, neither the specification nor the drawings indicate which end of the protein is the extracellular end. Furthermore, the claims do not require that the claimed polypeptide and variants have any particular conserved structure, or other disclosed distinguishing feature. The specification discloses that the nucleic acid encoding PRO4380 has (unspecified) homology to the nucleic acids which encode CER11H6_1, S56299, D89150_1, G70870, S43914, LMO34616_5, LLU78036_1, AF055904_2, P W79066 and ARGE_ECOLI, however the instant specification fails to indicate the degree of homology or whether the PRO4380 protein has any homology thereto.

The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequence and because the claims have no functional limitation. An enabling description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, polypeptides comprising the sequence of SEQ ID NO:57 or active or antigenic fragments thereof, but not the full breadth of the claims meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22 – 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims that recite "the extracellular domain" of the protein are indefinite as no extracellular domain has been described. Therefore, the metes and bounds of the claims cannot be determined. For example, see Claim 22, parts (c) and (d). It is noted that a putative transmembrane domain is disclosed in Figure 57 of the specification; however, it is clear from the disclosure that there is no conception of whether PRO4380 is in fact a transmembrane protein, and accordingly, which end of the protein would be the 'extracellular' domain. Therefore the term "the extracellular domain" is indefinite as it is not clear to which extracellular domain applicant intends to refer. Finally, if the protein had an extracellular domain, the recitation of "the extracellular domain. . .lacking its associated signal sequence" (claim 22, part

(d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell (see Alberts et al., p. 582).

The remaining claims are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 22 – 27, 29 - 31, 33, and 34 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruben et al. (WO 99/58660, published 18 November 1999, pp. 81 – 82 of the sequence listing). Ruben et al. teach a sequence, SEQ ID NO:131, which is 99.6% identical to SEQ ID NO:57 of the instant application. The sequence meets the limitations of claims 22 – 26, which are drawn to polypeptides at least 80% to 99% identical to SEQ ID NO:57. Applicant has identified residues 1 – 26 as the signal peptide (see Figure 26). Since the sequence from Ruben et al. is 100% identical to SEQ ID NO:57 starting at residue 16, the prior art sequence also meets the limitations of claims 27, 29, and 31, drawn to polypeptides comprising SEQ ID NO:57 lacking its associated signal sequence, independent of which end of the polypeptide is the extracellular domain. Similarly, the teachings of Ruben also anticipate claims 27 and 30, which are drawn polypeptides comprising the extracellular domain of SEQ ID NO:57. As mentioned previously in the rejection under 35 U.S.C. § 112, second paragraph, signal sequences are cleaved from proteins as they are processed. Therefore, the sequence from Ruben et al. comprises the extracellular domain of SEQ ID NO:57, as the two are 100% identical with the exception of the signal sequence.

Conclusion

No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHARON TURNER, PH.D.
PRIMARY EXAMINER

Daniel E. Kolker, Ph.D.

March 4, 2005